ORIGINAL RESEARCH

Patient Preferences Regarding Rheumatoid Arthritis Therapies: A Conjoint Analysis

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BACKGROUND: Tofacitinib, an oral Janus kinase inhibitor approved for the treatment of rheumatoid arthritis (RA), provides patients with an alternative to subcutaneously or intravenously administered biologic disease-modifying antirheumatic drugs (DMARDs). Little is known about patient preference for novel RA treatments.

OBJECTIVE: To investigate patient preferences for attributes associated with RA treatments.

METHODS: A choice-based conjoint survey was mailed to 1400 randomly selected commercially insured patients (aged 21-80 years) diagnosed with RA, who were continuously enrolled from May 1, 2012, through April 30, 2013, and had ≥2 medical claims for *International Classification of Diseases, Ninth Revision, Clinical Modification* diagnosis code 714.0 and no previous biologic DMARD use. Treatment attributes included route of administration; monthly out-of-pocket cost; frequency of administration; ability to reduce daily joint pain and swelling; likelihood of serious adverse events; improvement in the ability to perform daily tasks; and medication burden. Mean attribute importance scores were calculated after adjusting for patient demographics (eg, age, sex, years since diagnosis) using a hierarchical Bayes model. Patient preferences for each treatment attribute were ranked by the importance score. Part-worth utilities (ie, preference scores) were used to perform a conjoint market simulation.

RESULTS: A total of 380 patients (response rate, 27.1%) returned the survey. Their mean age (± standard deviation) was 54.9 (± 9.3) years. Nonrespondents were 2 years younger (mean, 52.9 years; $P = .002$) but did not differ significantly from respondents in known clinical characteristics. After adjustment for demographic characteristics, mean patients' ranking of treatment attribute importance, in decreasing order, was route of administration, 34.1 (± 15.5); frequency of administration, 16.4 (± 6.8); serious adverse events, 12.0 (± 9.3); cost, 10.1 (± 6.2); medication burden, 9.8 (± 8.2); joint pain reduction, 8.9 (± 3.8); and daily tasks improvement, 8.8 (± 4.7). For the route of administration attribute, the part-worth utility was highest for the oral route. Conjoint simulation results showed that 56.4% of respondents would prefer an oral route of administration.

CONCLUSION: Based on this survey completed by 380 patients with RA, commercially insured patients with RA consider the route of administration to be the most important attribute of their RA treatment. In this study, the majority (56.4%) of patients preferred the oral route of administration over other routes. Understanding patient preferences may help to inform provider and payer decisions in treatment selection that may enhance patient adherence to therapy.

Stakeholder Perspective, page 93

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Health professionals are increasingly encouraged to involve patients in their treatment decisions, recognizing that patients are experts in terms of their preferences and have unique knowledge of their own health.[1-5] In 2010, the Affordable Care Act created the Patient-Centered Outcomes Research Institute (PCORI), which stresses the importance of patient-centeredness care.[6] Patient-centeredness care refers to the need to address patient preferences, patient decision-making needs, and characteristics of patients. This

emphasis on increased understanding of patient preferences and their incorporation into treatment decisions has been driven by the improvement associated with patient care and treatment satisfaction when patients' perspectives are taken into consideration.[7,8]

For patient preferences to be used effectively in the delivery of healthcare, it is important to understand the desire for specific treatment attributes that shape affinities for particular therapeutic medications. With respect to rheumatoid arthritis (RA), current therapies include conventional synthetic disease-modifying antirheumatic drugs (DMARDs), biologic DMARDs, and targeted synthetic DMARDs, including the new therapeutic class of Janus kinase (JAK) inhibitors.[9] These therapies vary in their mechanisms of action; they also differ in the route and frequency of their administration.

Previous RA research has addressed patient preferences for features associated with conventional synthetic and biologic DMARDs.[10-12] These studies have produced a broad range of results, in part as a result of the dependence of the description of the drug features that were provided to a study participant.[13] A 2004 study by Fraenkel and colleagues showed that patients preferred the biologic DMARD etanercept over conventional synthetic DMARDs, partially because of its favorable adverse event profile[10]; however, for their study, the copayment amounts associated with etanercept were presented to the study patients as being equal to, or only slightly higher than, the copayments associated with conventional synthetic DMARDs.[10] This action of leveling the cost-sharing amount between drugs essentially negated cost as an important differentiator between the drugs.

A more recent study by Augustovski and colleagues, published in 2013, addressed the preferences of patients in Argentina for biologic DMARDs used in RA, showing that cost was the most important treatment attribute, followed by systemic adverse effects, frequency of administration, efficacy, route of administration, local adverse events, and serious infections.[11]

Route of administration may be an important differentiator between drugs that are used to treat RA, especially if patient preferences influence adherence and outcomes of therapy. Various medication attributes may factor into medication delivery preference, such as administration time, ease of administration, and fear of needles. Little is known about the relative importance of treatment attributes in RA since the addition of oral medications, such as targeted synthetic DMARDs, to the list of available therapies. The goal of our study, which used a conjoint analysis methodology, was to ascertain relative patient preferences associated with the route of administration and other attributes of biologic DMARDs and targeted synthetic DMARDs in the treatment of patients with RA.

KEY POINTS

- Little is known about patients' preferences for specific attributes of RA medications.
- A new survey evaluated patients' preferences for the route of administration, frequency of administration, cost, medication burden, ability to reduce daily joint pain or swelling, likelihood of serious adverse events, and improvement in ability to perform daily tasks.
- In this survey of 380 patients with RA, the attribute with highest score on importance was the route of administration, followed by frequency of administration, serious side effects, monthly cost-sharing, medication burden, ability to reduce joint pain/swelling, and improvement in daily activity.
- It is not surprising that efficacy and safety are not the most important attributes for patients with chronic conditions that require long-term therapy, especially if available treatments have similar efficacy and safety.
- Oral administration of a drug was the most often selected preferred route, and once every 8 weeks was the preferred frequency of administration.
- Improved understanding of patients' preferences for medication attributes may enhance more prudent treatment decisions by prescribers and payers.
- This may result in greater patient satisfaction and higher treatment adherence rates.

Methods

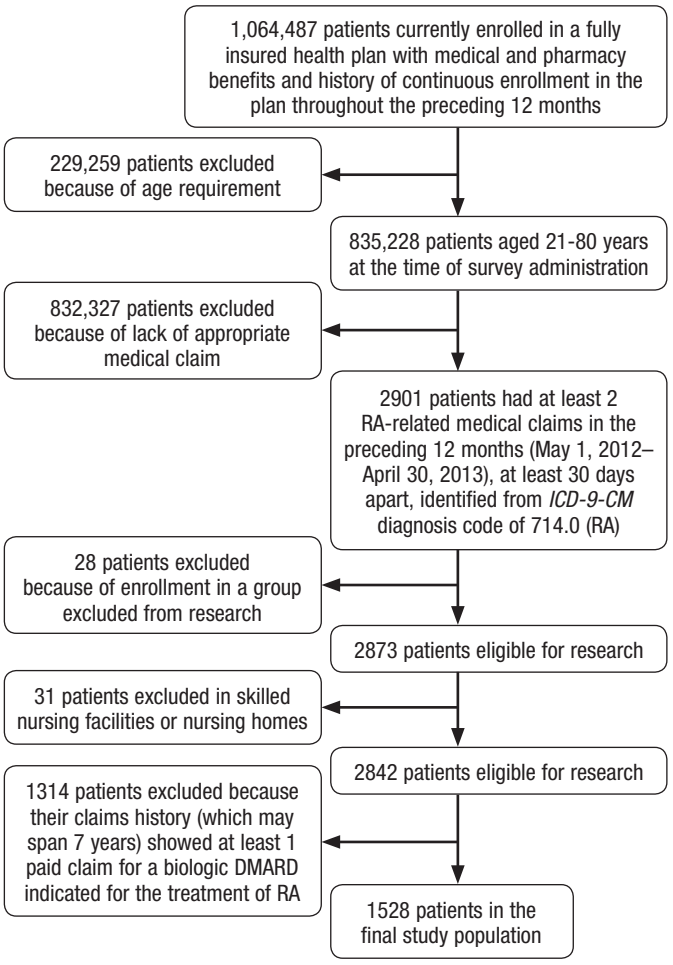
Study Design

A cross-sectional postal survey of patients with RA was conducted to ascertain the relative importance of individual drug attributes, including safety; efficacy; cost; and mode, method, and frequency of administration, in determining patient preferences for specific therapies for RA. A choice-based conjoint analysis was used to determine the relative importance of individual attributes for the medications of interest.[13-15] Patients were blinded to the medication names; only the relevant attributes for each medication were listed in the survey.

Patient Population

For participation in the study, patients had to be aged 21 to 80 years at the time of survey administration, be currently enrolled in a fully insured Humana commercial health plan with medical and pharmacy benefits, and to have had at least 2 RA-related medical claims in the previous 12 months, at least 30 days apart, as identified by *International Classification of Diseases, Ninth*

Figure Study Population Selection Process



DMARD indicates disease-modifying antirheumatic drug; *ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification*; RA, rheumatoid arthritis.

Revision, Clinical Modification diagnosis code 714.0 (rheumatoid arthritis).

Patients were excluded from the study if they were enrolled in administrative services–only groups (which are excluded from research according to Humana policy), resided in a nursing home, were eligible for low-income subsidies, or had evidence of a paid claim for tofacitinib or for a biologic DMARD indicated for RA, psoriasis, psoriatic arthritis, or ankylosing spondylitis at any time during their health plan enrollment before the mailing of the survey.

Survey Design

To generate the survey for the conjoint analysis, the key attributes associated with the range of treatments of interest (ie, biologic DMARD therapies and tofacitinib) were identified, followed by the assignment of various levels for the treatment attributes. The survey included 10 choice tasks, and each choice task included 2 medication concepts (drug A and drug B), where a medication concept was defined by a specific combination of attributes chosen randomly, using Sawtooth SSI Web software (version 8.2; Sawtooth Software, Inc, Sequim, WA). Ten choice tasks was identified as the threshold to maximize the efficiency of the survey design, based on the number of attributes that defined the concept (7 attributes per concept) but would not lead to respondent fatigue.

Because the survey was aimed at generating insight about patient treatment preferences, respondents were not given the option to select "none" within the choice task. Each concept was generated randomly, and repeated concepts were not included in the survey design. The attributes were listed randomly in each survey version to mitigate ordering bias (for a version of the survey see **Appendix** at www.AHDBonline.com).

The final survey contained 2 sections, including (1) general questions regarding the respondent's medical history related to RA, and (2) the choice-based conjoint question section described above. Four versions of the choice-based conjoint component were generated; each version of the questionnaire contained the same questions but in a different sequence. Survey versions were assigned randomly, and participants were asked to choose the most preferred drug among the alternatives in each 2-profile choice set. The conjoint portion of the survey was designed with Sawtooth software, using a generic choice design. This software was used to help generate a survey of appropriate length, given the number of attributes and their levels of interest. An internal pretesting process involving 4 independent research and nonresearch staff, as well as Humana's formal Member Communications review, was conducted to evaluate the clarity, organization, readability, and time burden of the instruments. The survey was approved by an independent Institutional Review Board.

A 4-wave survey rollout process was used to optimize the survey response rate. The first-wave mailing, sent to patients on August 30, 2013, consisted of an advance-notice alert in the form of a brief letter. The purpose of the first-wave mailing was to inform potential participants that they would be receiving a study questionnaire and to explain the purpose of the study. The second-wave mailing, sent to patients on September 6, 2013, consisted of the survey instrument, an appropriate cover letter and consent form, as well as a self-addressed stamped envelope to facilitate response. One week later, on September 13, 2013, a follow-up reminder postcard was sent to potential participants. The fourth-wave mailing, on September 27, 2013, was sent only to nonrespondents. A copy of the survey instrument was included along with a

reminder letter. The period of survey administration or collection was 8 weeks from the date of the advance-notice mailing to the closure of survey collection. Respondents were provided with a $10 gift card for their time and effort in completing the survey.

Statistical Analysis

Descriptive statistics were used to summarize demographic and clinical characteristics of the study sample, obtained from administrative claims data and from responses to the first 4 survey questions, which pertained to joint history, length of time with symptoms, length of time since diagnosis, and whether the survey was being completed by the patient or by someone else. The administrative claims data included age, sex, geographic region, and the RxRiskV score, which is a prescription claims-based comorbidity index originally developed as an enhancement of the RxRisk risk assessment instrument for the Veterans Health Administration population.[16-18] The RxRiskV score is determined based on the identification of 45 distinct comorbid conditions via their associated medication treatments (score range, 0-45). Two-sample *t*-tests and chi-square tests were used to compare descriptive statistics between respondents and nonrespondents.

The results of the conjoint analysis were analyzed to determine relative preference for each attribute (ie, order of attribute importance). An importance score reflects the effect that each attribute had on the choice made, given the range of levels included in the questionnaire. The preference for each level within an attribute was evaluated by counting the number of times the level was chosen relative to the number of times it was offered, to estimate the main effects and joint effects of the attributes, where joint effects were evaluated by the number of times medication concepts were chosen: when attributes were listed together as part of the same medication concept. The Sawtooth software calculated the number of times that an attribute level was chosen relative to the number of times it was available for choice. The software also calculated a chi-square test value for each main effect and joint effect. The test is termed "within-attribute chi-square" and indicates whether levels of a particular attribute differ significantly in frequency of choice within the respective attribute.

The influence of demographic and clinical characteristics on each attribute was assessed using hierarchical Bayesian estimation, which allows for part-worth utilities (ie, attribute-level utilities), with a higher score for a level indicating greater desirability or preference (utility). This set of utilities was calculated at the individual patient level, thus overcoming the limitation associated with having only aggregate data available after a conjoint analysis. The part-worth utility data were then used to perform conjoint simulations to predict share of preference for tofacitinib and for biologic DMARDs, representative of medications routinely used in clinical practice for the treatment of RA.

Table 1 Baseline Demographic and Clinical Characteristics of Patients Diagnosed with Rheumatoid Arthritis: Survey Respondents versus Nonrespondents

Measure	Survey respondents (N = 380)	Survey nonrespondents (N = 1020)	*P* value
Age, yrs, mean (SD)	54.9 (± 9.3)	52.9 (± 10.9)	.0016
Age category, yrs, N (%)			
20-29	<10	33 (3.2)	.0150
30-39	25 (6.6)	91 (8.9)	
40-49	63 (16.6)	203 (19.9)	
50-59	158 (41.6)	414 (40.6)	
60-69	114 (30.0)	235 (23.0)	
70-79	16 (4.2)	39 (3.8)	
80-89	<10	<10	
Sex, N (%)			
Male	70 (18.4)	225 (22.1)	.1377
Female	310 (81.6)	795 (77.9)	
Geographic region,[a] N (%)			
Midwest	134 (35.3)	270 (26.5)	.0133
South	229 (60.3)	705 (69.1)	
RxRiskV comorbidity score, mean (SD)	5.2 (± 2.9)	5.1 (± 3.0)	.7201
History of injection/infusion utilization, N (%)	136 (35.8)	373 (36.6)	.7875
Years since diagnosis of rheumatoid arthritis, mean (SD)	9.2 (± 9.2)		
Median [range]	6.0 [0.0-57.0]		
Years since first experienced symptoms of rheumatoid arthritis, mean (SD)	11.2 (± 10.2)		
Median [range]	8.0 [0.0-58.0]		
Joint surgery associated with rheumatoid arthritis, N (%)	37 (9.7)		
Person who completed the survey, N (%)			
Self	371 (97.6)		

[a]In the United States. Information for the Northeast and the West is not reported, in compliance with HIPAA privacy rules.
SD indicates standard deviation.

Table 2 Choice-Based Conjoint Count Analysis of Medication Attributes

Medication attributes and levels	Proportion of times a concept containing the attribute level was selected[a]	Within-attribute chi-square value[b]	Degrees of freedom	*P* value
	Usable surveys (N = 363)			
Route of administration				
Oral	0.754			
By self-injection	0.492	566.57	2	<.01
By infusion	0.263			
Frequency of administration				
Twice daily	0.410			
Once weekly	0.534			
Every other week	0.488	49.77	3	<.01
Once every 8 weeks	0.567			
Chance of serious side effects				
4 of 100 people	0.551			
6 of 100 people	0.527	43.50	2	<.01
8 of 100 people	0.424			
Monthly cost to you (commercial)				
$25 copay	0.573			
$50 copay	0.536	83.89	2	<.01
$75 copay	0.394			
Ability to reduce daily joint pain and joint swelling				
50 of 100 people	0.519			
52 of 100 people	0.461	8.67	3	<.05
54 of 100 people	0.497			
58 of 100 people	0.524			
Improvement in ability to perform daily tasks and activities				
32%	0.500			
33%	0.471	5.55	3	Not significant
34%	0.502			
36%	0.527			
Medication burden (take with another medication)				
No	0.588	110.65	1	<.01
Yes	0.412			

[a]Among the number of times the concept was presented as a possible choice by a survey respondent.

[b]The within-attribute chi-square test for each main effect indicates whether levels of the respective attributes differ significantly in their frequency of choice within the respective attribute.

Results

Participating Patients' Characteristics

The attrition flow diagram portrayed in the **Figure** summarizes the inclusion and exclusion criteria used to determine the final sample from which survey participants were randomly selected. After exclusion for age (outside range), absence of a relevant medical claim, enrollment in a group excluded from research, residence in a nursing home, or a paid claim for a biologic DMARD indicated for the treatment of RA, the sample size was 1528 patients, from which 1400 patients were randomly selected to receive the survey.

Table 1 compares survey respondents and nonrespondents. A total of 380 patients returned the survey, representing a 27.1% response rate. The average age of respondents was 54.9 (standard deviation [SD], 9.3) years. The majority (81.6%) were female, and most resided in either the South (60.3%) or the Midwest (35.3%). Approximately 36% (136 of 380) had received injection or infusion of a non-RA medication in the preceding 180 days, and their average RxRiskV score was 5.2 (SD, 2.9). A comparison of patients who responded to the survey and those who did not respond revealed significant differences between the groups in terms of age and geographic region of residence (both P <.05). No significant differences between these groups were found in sex distribution, RxRiskV comorbidity score, or history of injection or infusion.

The results indicated that respondents were diagnosed with RA an average of 9.2 (SD, 9.2) years before receiving the survey, and their symptoms began an average of 11.2 (SD, 10.2) years before the study (Table 1). Approximately 10% (37 of 380) of respondents indicated that they had undergone joint surgery because of RA.

Choice-Based Conjoint Analysis

Of the 380 patients who returned the survey, 363 (95.5%) completed all or some of the choice-based conjoint section. **Table 2** shows the proportion of times that levels within an attribute were selected by survey respondents. Differences in frequency of choice of levels for all attributes were observed, with the exception of improvement in the ability to perform daily tasks and activities. The most frequently selected route of administration was the oral route, and once every 8 weeks was the most preferred frequency of administration.

Respondents most often chose the lowest copayment, the lowest incidence of serious side effects, and the highest likelihood of clinical benefit (efficacy). In addition, respondents were more likely to select the option that did not require adding another medication (typically methotrexate) to their current therapy regimen (P <.01).

A summary of the scores for utility and attribute importance to respondents was generated from the hierar-

chical Bayes models (**Table 3**). These models estimate the part-worth for each individual versus aggregate estimates (average utility) generated by the logit method.

Overall, the relative importance of attributes (ie, mean relative importance score ± SD) for respondents, from highest to lowest, was route of administration (34.1 ± 15.5), frequency of administration (16.4 ± 6.8), chance of serious side effects (12.0 ± 9.3), monthly cost-sharing requirement (10.1 ± 6.2), medication burden (9.8 ± 8.2), ability to reduce daily joint pain and joint swelling (8.9 ± 3.8), and improvement in the ability to perform daily tasks and activities (8.8 ± 4.7).

Conjoint Market Simulations

As a final step in the analysis, the part-worth utilities derived from the hierarchical Bayes models were applied to medication concepts based on several medications currently available for the treatment of RA. We simulated preference shares based on medication attributes, as reported in **Table 4**. The simulation base-case scenario took into account data on drug efficacy and safety derived from the prescribing information[19-22] and from a separate meta-analysis of available drugs.[23] Improvement in daily living activities was based on the same independent meta-analysis of available drugs.[23]

Out-of-pocket cost of $65 was assumed for all patients, which is the median amount for the Humana commercial plan member population treated with these medications during the study period (Table 4). This median estimate was based on member out-of-pocket costs from medical and pharmacy claims for biologic DMARDs. Office-visit costs for administering those biologic DMARDs in a clinical setting were not included in the estimate; however, such amounts were minor in relation to the total billed amount (health plan plus member share) for the medication.

When comparing the various drugs, the range of some responses by medication was relatively narrow. For example, the range of reduction in joint pain was 50% to 58%, and for serious adverse events, the range was 4% to 8%. This doubling in the likelihood of serious side effects resulted in this attribute ranking third highest in the utilities and importance summary (Table 4).

Sensitivity Analysis

A sensitivity analysis was performed with the assumption that measures for specific medication categories were the same throughout the population. This included, for example, the medication's ability to reduce joint pain (58% for all), improvement in activities of daily living (36% for all), and the likelihood of serious adverse events (8% for all). This approach examined the difference in patient preference share derived solely from the

Table 3 Choice-Based Conjoint Utilities and Importance Summary[a,b]

Medication attributes and levels	Average utility[c]	Standard deviation	Average importance	Standard deviation
Route of administration				
Oral	99.3	72.2	34.1	15.5
By self-injection	7.3	57.2		
By infusion	–106.6	82.8		
Frequency of administration				
Twice daily	–51.9	38.9	16.4	6.8
Once weekly	3.6	22.0		
Every other week	3.9	21.5		
Once every 8 weeks	43.8	40.6		
Chance of serious side effects				
4 of 100 people	24.7	47.8	12.0	9.3
6 of 100 people	6.6	13.6		
8 of 100 people	–31.4	41.8		
Monthly cost to you (commercial)				
$25 copay	26.1	31.2	10.1	6.2
$50 copay	3.4	19.3		
$75 copay	–29.5	27.6		
Medication burden (take with another medication)				
No	29.8	33.0	9.8	8.2
Yes	–29.8	33.0		
Ability to reduce daily joint pain and joint swelling				
50 of 100 people	–7.5	25.3	8.9	3.8
52 of 100 people	4.6	23.0		
54 of 100 people	–6.5	28.1		
58 of 100 people	9.5	24.3		
Improvement in ability to perform daily tasks and activities				
32%	–4.1	23.7	8.8	4.7
33%	–9.1	26.0		
34%	–0.7	29.4		
36%	13.9	23.5		

[a]The relative importance of each medication attribute is characterized by considering how much difference each attribute could make in the total utility of a medication. That difference is the range in the attribute's utility values. Percentages are calculated from relative ranges, obtaining a set of attribute importance values that total 100%. The higher the score, the greater the attribute's importance to respondents.
[b]Clinical and demographic covariates were included to adjust for differences in respondent characteristics. Clinical covariates included years since diagnosis of rheumatoid arthritis, years with symptoms, previous joint surgery, RxRiskV, and infusion in previous 180 days. Demographic covariates included age, sex, and region.
[c]The sum of average utilities within an attribute is set to equal zero.

Table 4 Simulation Base-Case Scenario for Medication Concepts

	Tofacitinib	Adalimumab	Etanercept	Infliximab
Route of administration	Oral	Subcutaneous	Subcutaneous	Infusion
Frequency of administration	Twice daily	Every 2 weeks	Weekly	Every 8 weeks
Reduction of joint pain, %	54[a,b]	58[b,c]	52[b,d]	50[b,e]
Improvement in ability to perform daily tasks and activities,[b] %	36	34	33	32
Serious adverse events, %	4[a,b]	8[b,c]	4[b,d]	6[b,e]
Medication burden (ie, take with another medication)	No[a]	No[c]	No[d]	Yes[e]
Patient out-of-pocket cost, $[f]	65	65	65	65

[a]Xeljanz (tofacitinib) tablets prescribing information; June 2015. According to the prescribing information, this medication may be used as monotherapy or in combination with methotrexate or other nonbiologic disease-modifying antirheumatic drugs. For purposes of this study, tofacitinib was assumed to be used as monotherapy.
[b]Vieira MC, et al. *Ann Rheum Dis*. 2012;71(suppl 3). Abstract FRI0185.
[c]Humira (adalimumab) injection prescribing information; November 2015.
[d]Enbrel (etanercept) prescribing information; March 2015.
[e]Remicade (infliximab) prescribing information; October 2015.
[f]US dollars.

Table 5 Patient Preference Shares for Simulation Base-Case and Alternative Scenarios[a]

	Tofacitinib, %	Adalimumab, %	Etanercept, %	Infliximab, %
Base case[b]	56.4	14.0	25.5	4.2
Alternative[c]	54.1	17.4	18.1	10.1

[a]The total for each horizontal row should be 100% (± rounding error).
[b]The base case assumes all medication attributes shown in Table 4.
[c]The alternative case assumes all efficacy and safety attributes to be the same between medication concepts, with differences only in method of administration, frequency of administration, medication burden: ability to reduce joint pain (58% for all), improvement in activities of daily living (36% for all), and chance of serious adverse events (8% for all).

method of medication administration, frequency of administration, and medication burden. Under these conditions, the analysis showed similar results for the base-case scenario and the alternative scenario for tofacitinib (56.4% base analysis vs 54.1% sensitivity analysis) and adalimumab (14.0% vs 17.4%), with greater differences observed between scenarios for etanercept (25.5% vs 18.1%) and infliximab (4.2% vs 10.1%; **Table 5**).

Discussion

Our study provides insight into medication attributes that are relevant in determining patient choice among currently available treatments for RA. The results show that the route of administration was the most important medication attribute, with the oral route being the preferred choice. The oral route of administration was not included in the medication attribute choices for biologic DMARDs in the survey by Huynh and colleagues; in that survey, respondents were restricted to choose between self-injection at home and intravenous administration in a clinic.[12] Of note, patients who had not yet been treated with biologic DMARDs chose self-injection at home as their preferred route of administration. These patients cited the desire to minimize time associated with transportation and treatment as the most common reason for that choice.[12]

In our study, cost was not 1 of the 3 most important medication attributes to survey respondents, all of whom were enrolled in a commercial health plan. Cost values in our survey ($25-$75) were fairly consistent with the payments made by patients in Humana's commercial population at the time of this study (median, $65), according to claims data, which may have influenced the relative ranking of the cost attribute.

By contrast, Augustovski and colleagues, who conducted a discrete choice experiment among patients with RA in Argentina, found cost to be the most important attribute, followed by systemic adverse effects, frequency of administration, efficacy, route of administration, local adverse events, and serious infections.[11] In that study, the 3 choices for monthly out-of-pocket costs were ₱0, ₱500, and ₱1500 (₱ = Argentine pesos; for context, approximately two-thirds of that sample reported a monthly income of ₱949-₱4041).[11] Although these findings are not necessarily relevant for a commercially insured population in the United States, cost may be a more important factor for people aged 65 years and older potentially living on fixed incomes in the United States, as indicated by a similar study focused on Humana's Medicare members.[24]

Although the cost attribute was not as significant as the route or frequency of administration in the present study, it did rank higher than some efficacy measures. Efficacy might have been selected as an important attribute with less frequency, because the range of choices was relatively narrow; that is, the medication choices were similarly effective. Positive responses for ability to reduce joint pain

and joint swelling ranged from 50% to 58%, and positive responses for improvement in the ability to perform daily tasks and activities ranged from 32% to 36%.

By contrast, Schaarschmidt and colleagues, who conducted a conjoint analysis of treatment preferences among patients with moderate to severe psoriasis, found that the efficacy measure "chance of experiencing significant reduction in my psoriasis" ranked second highest, after "treatment location" (ie, where treatment is administered), and followed by "method of delivery."[25] In their study, the efficacy attribute ranged from 40% to 100%,[25] consistent with the hypothesis that a wider range of attribute levels may result in patients choosing the preferred level of an attribute with greater frequency.

The efficacy measures for our study were carefully chosen based primarily on data from randomized controlled trials; the efficacy measures for biologic DMARDs in the treatment of RA have been reported to be similar.[26-28] It is not surprising that medication attributes other than efficacy and safety increase in importance for patients with chronic conditions that require long-term continual treatment, especially if the drugs in question have similar efficacy and safety features.

Taking patient preferences into consideration may result in reordering the ranking of known factors deemed important by physicians in determining the right treatment for each patient. A few qualitative studies indicate that patient approaches to care differ from those of physicians, and that patients are increasingly involved in the decision-making regarding their care.[5,29] For example, in a study comprised of interviews with senior rheumatologists in Sweden, several physicians noted that their patients were well-educated and demanded that their preferences and requests for specific biologic DMARDs be taken into consideration.[5]

Patient involvement in medical decision-making has also been associated with greater satisfaction and, in turn, greater adherence to treatment. This is supported in research by Kjeken and colleagues, who reported that among patients with RA, satisfaction was greater for those with high (vs low) involvement in medical decisions (91% vs 61%, respectively; P <.001).[7] Moreover, from a literature review of preferences of patients with RA, Barton concluded that patient preferences for mode and frequency of treatment administration were important factors that affected their medication adherence.[8] Soliciting these preferences from patients may encourage them to become more adherent sooner rather than later.[30]

Limitations

Limitations common to studies involving survey methodology apply to this study as well, including the potential bias because of nonresponse. The comparison of respondents and nonrespondents indicated significant differences in 2 demographic characteristics—age and geographical region; however, no significant differences were found in clinical characteristics between these groups.

We could not determine whether significant differences existed between respondents and nonrespondents for several variables (ie, years since onset of symptoms, years since diagnosis, and history of joint surgery associated with RA), which potentially increased the nonresponse bias. These variables were not captured sufficiently, because administrative claims data do not encompass the full history of a patient's lifetime.

It is possible that respondents differed from nonrespondents in other (unmeasured) characteristics, such as the ability to understand the survey questions and the tasks involved in completing the survey. Moreover, the length of the survey might have influenced the responses because of possible fatigue or loss of concentration, which might have placed some individuals at risk of failing to make rational choices. However, where there was a clear order among levels in an attribute, such as cost, the results indicated that individuals were attentive when completing the survey.

This survey was intended to be distributed to patients who had been diagnosed with RA and had never used a biologic DMARD to treat their RA. Because we used health insurance claims data for this study, missing data might have contributed to misclassification bias with respect to diagnosis and medication history.

In addition, the results of this study are a function of the levels of the attributes included in the survey instrument; as such, the results cannot be extrapolated to other attributes or levels. Even among the survey respondents, average utilities of the levels of an attribute are interpretable within a particular attribute and are not to be interpreted between levels of different attributes.

Conclusion

Based on survey responses in this study, the route of administration of a medication is an important consideration for patients diagnosed with RA who have not received any biologic DMARD therapy. Furthermore, based on these results, the majority of patients with RA would prefer the use of a medication with oral route of administration. Given the variety of RA therapies available in the marketplace, gaining better understanding of the attributes that commercially insured patients prefer most about their medications may help to inform prescriber and payer decisions for selecting therapies that will lead to greater patient satisfaction and improved medication adherence. ■

Continued

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STAKEHOLDER PERSPECTIVE

Challenges in the Assessment of Patient Preferences among RA Therapies

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The selection of appropriate therapy, including optimal sequencing therapy for rheumatoid arthritis (RA), is top of mind for all stakeholders. The number of Americans with RA is expected to increase by almost 30% by 2020.[1] The cost of treating RA in the United States is expected to increase from the current $6.4 billion to $9.4 billion by 2020.[2]

The wholesale acquisition cost (WAC) inflation for agents for inflammatory conditions, including RA, is one of the highest of all therapeutic areas among common diseases. For example, based on Medi-Span data, the WAC per unit of tofacitinib (Xeljanz) 5 mg was $34.25 on January 1, 2013, and $52.82 on January 1, 2016.[3] On these dates, the WAC per unit of adalimumab (Humira kit) 20 mg/0.4 mL was $1024.32 and $1727.53, respectively; the WAC per unit of etanercept (Enbrel) 50 mg/mL was $527.59 and $951.18; and the WAC per unit of infliximab (Remicade) 100 mg was $773.97 and $1,021.43.[3] These WAC per unit prices do not reflect cost per day, month, or year. These price changes during this 3-year period represent a cost increase of 54%, 67%, 80%, and 32% for the respective drugs.

PATIENTS/PAYERS: In the article by Louder and colleagues in this issue, the authors discuss patient preferences for RA therapies based on package insert data, concluding that the efficacy is similar among the 4 medications discussed.[4] What they do not reference are long-term data that evaluate disease progression. Patient preference of a medication attributes might have been different if the study included a question related to a medication's ability to prevent or slow long-term disease progression rather than based on symptoms only. Symptom improvement, activities of daily living, and radiographic progression are all important factors when considering coverage options.

The authors state that patient preference and satisfaction may lead to increased treatment adherence rates. A gap not answered in this questionnaire is real-world experience; that data may be available in a real-world setting. Comparing initial patient preference before therapy, then evaluating real-world adherence based on claims data may be very telling regarding real and perceived benefits of initial preference. Another data point of interest may be to evaluate the initial preference for route of administration based on a questionnaire such as the one in this study compared with patient preferences after an initial visit with a rheumatologist to discuss the pros and cons of different routes and frequency of administration. This may help answer if the initial patient preference is consistent with the preference after an initial discussion.

However, the majority of payers need to manage the inflammatory class of medications as a whole, including all their indications, beyond RA, such as psoriasis and others. This contributes to the inability of payers to make coverage requirements based on 1 factor alone (eg, patient preference) for the entire inflammatory medication class.

PROVIDERS: Providers need to consider several factors when recommending and prescribing expensive medications such as biologic disease-modifying antirheumatic drugs (DMARDs) or an oral JAK inhibitor. Because no oral agents dosed every 8 weeks are currently available, other factors should be considered, including published data evaluating efficacy and safety in short-term controlled trials, long-term observational data, as well as past experience with the individual agents. These considerations are taken into account when discussing treatment options with individual patients to determine the optimal initial therapy, and biologic therapy or non-traditional, oral DMARD therapy.

Although patients may have a preference for a certain route or frequency of administration, payer coverage criteria may limit the prescribing options for initial therapy. These coverage limitations reflect the pressure to balance patient preference, efficacy, safety, and fiscal responsibility, because patients, providers, and payers are unable to control the WACs set by manufacturers. ■

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